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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/527,426	03/10/2005	Yu Momose	3094US0P	7181

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EXAMINER	
LOEWE, SUN JAE Y	

ART UNIT	PAPER NUMBER
1609	

MAIL DATE	DELIVERY MODE
04/30/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/527,426	MOMOSE ET AL.	
	Examiner	Art Unit	
	Sun Jae Y. Loewe	1609	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26 and 28* is/are pending in the application.

4a) Of the above claim(s) *26 and 28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-21* is/are rejected.

7)☒ Claim(s) *1-16 and 22-25* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/10/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I (claims 1-25) and species of example 337 in the reply filed on February 28, 2007 is acknowledged.

Based on Applicant's election, the search and examination was performed for a core chemical structure wherein the limitations were: R^1 = oxazolyl; A = phenyl; z = $-O(CH_2)_n-$ or $-(CH_2)_n-O-$ (where $n \geq 1$); B = pyrazole; R_2 = thiazolyl or $-PO(OR^9)(OR^{10})$. The other variables (X, Q, Y, W, V) were allowed to assume the full scope of the definition provided in claim 1.

MPEP 1893.03(d) states that when all of the claims drawn to the elected invention are allowable (i.e., meet the requirements of 35 U.S.C. 101, 102, 103 and 112), the nonelected invention(s) should be considered for rejoinder. The instantly elected invention was not allowable under 35 U.S.C 112 (see below section 6). Thus, the nonelected subject matter was *not* rejoined. The search and examination was performed *only* for the elected subject matter defined above.

2. Claims 26 and 28 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected matter. Election was made **without** traverse in the reply filed on February 28, 2007. The requirement is still deemed proper and is therefore made FINAL.

Priority

3. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Information Disclosure Statement

4. The information disclosure statement (IDS) submitted on March 10, 2005 was in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement was considered. The following references were not considered because English language translations were not provided: WO J96/13264 and WO 03/000685-Abstract. A signed copy of form 1449 is enclosed herewith.

Claim Objections

5. Claims 1-25 are objected to for containing non-elected subject matter: (i) compounds of formula (I), pharmaceutical compositions and prodrugs thereof, not meeting the structural limitations set forth in section 1.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 17-21 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the preparation of pharmaceutical compositions for the treatment of diabetes mellitus, insulin resistance, and obesity, does not reasonably provide enablement for the preparation of pharmaceutical compositions for the treatment of hyperlipidemia, hypertension, impaired glucose tolerance. The specification also does not provide enablement for the preparation of pharmaceutical compositions for the prophylaxis of diabetes mellitus,

hyperlipidemia, impaired glucose tolerance, or obesity. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The standard for determining whether the specification meets the enablement requirement was cast in the Supreme Court decision of *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916) which postured the question: is the experimentation needed to practice the invention undue or unreasonable? That standard is still the one to be applied. *In re Wands*, 858 F.2d 731, 737, 8USPQ2s 1400, 1404 (Fed. Cir. 1988). MPEP 2164.01(a) states "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue". The factors are applied below to the instant claims.

The breadth of the claims
The claims are drawn to pharmaceutical compositions, that include compounds of formula (I), that are agents for the treatment/prophylaxis of diabetes mellitus, hyperlipidemia, impaired glucose tolerance, obesity, hypertension, and insulin resistance. Because a specific definition for "prophylaxis" was not provided in the specification, the art recognized definition - "the preventing of a disease" (http://dictionary.reference.com/browse/prophylaxis/p.1) – was applied herein for the purpose of this examination.

The nature of the invention
Compounds of formula (I) are disclosed to possess PPAR γ binding and PPAR γ antagonistic activities.

The state of the prior art/level of ordinary skill/level of predictability
It is known in the art that a correlation exists between in vitro or in vivo PPAR γ antagonism and the treatment of diabetes, insulin resistance, and obesity (Rieusset et al., abstract). It is also known that a correlation exists between PPAR γ *agonism* and the treatment of hyperlipidemia (He et al., page 15717, 1st column, 5th paragraph), hypertension (Ryan et al., abstract), impaired glucose tolerance (Hung et al., abstract); however, such nexus does not exist in the art for the treatment of the stated diseases and PPAR γ *antagonism*.

Similarly, a nexus does not exist between PPAR γ antagonism and the *prevention* of diabetes, insulin resistance, obesity, impaired glucose tolerance, hyperlipidemia, and hypertension. To date, prevention of diabetes 1 is not possible. Prevention of diabetes 2 is possible through medication *in combination* with diet, exercise, and healthy lifestyle (http://diabetes.webmd.com/guide/preventing-type-2-diabetes). Prevention of prediabetes is possible through lifestyle changes (http://diabetes.webmd.com/tc/Prediabetes-Topic-Overview). Prevention of insulin resistance is possible through living a healthy lifestyle (http://diabetes.webmd.com/guide/insulin-resistance-syndrome). The use of medication by itself does not work to prevent obesity; the amount of calories burned must exceed the calories taken in (http://www.webmd.com/diet/tc/Obesity-Overview). Weight loss and physical activity are the best ways to prevent and manage hyperlipidemia (http://jcem.endojournals.org/cgi/content/full/90/3/0, page 3 of 4). Lastly, for hypertension, prevention occurs by a combination of: maintaining a healthy weight, getting exercise, reducing salt intake and reducing stress (http://www.webmd.com/hypertension-high-blood-pressure/guide/preventing-high-blood-pressure?page=2)

The amount of direction provided by the inventor/existence of working examples
The disclosure provides a method of preparing compounds of formula (I) that have PPAR γ antagonism and PPAR γ binding activity.

The quantity of experimentation needed to make or use the invention
In the absence of a nexus between PPAR γ antagonism and the treatment of hyperlipidemia/hypertension/impaired glucose tolerance one of ordinary skill would not be enabled by the instant disclosure to make the claimed agents for the treatment thereof.

In the absence of a nexus between PPAR γ antagonism and the prevention of the diseases disclosed one of ordinary skill would not be enabled by the instant disclosure to make the claimed agents for the prophylaxis thereof.

The skilled artisan would be unable to practice the invention commensurate with the scope of the claims without first making a substantial inventive step. The quantity of experimentation needed is undue.

Conclusions

7. No claims stand allowed.

8. Any inquiry concerning this communication should be directed to Sun Jae Y. Loewe, Ph.D. whole telephone number is 571-272-9074. The examiner can normally be reached on Monday through Friday from 7:30 am to 5:00 pm.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Cecilia Tsang (571) 272-0562, can be reached. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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